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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/646,763	10/24/2000	Michel Lanquetin	GEI-078	8985

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EXAMINER	
HUI, SAN MING R	

ART UNIT	PAPER NUMBER
1617	

DATE MAILED: 08/24/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/646,763	LANQUETIN ET AL.	
	Examiner	Art Unit	
	San-ming Hui	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 August 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3 and 5-18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3 and 5-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on August 8, 2006 has been entered.

Claims 1, 3, 5-18 are pending.

Examiner notes that the amendments filed August 8, 2006 replaces the limitation "with systemic effect" with "for quickly penetrating the patient's skin". The two limitations essentially describe the same effect, i.e., the drug is intended to penetrate through skin and enter the systemic circulation for treating hormonal deficiency. Therefore, in essence, the cited prior arts still render the herein claimed invention obvious.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 3, 5-8, 11, 12, 14-15, and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Saunal et al. (WO96/30000, English equivalent: USPN 6,010,716 is also provided), reference of record, and Maillo et al. (EP 0 785 211 A1) in view of Winters et al. (WO95/30409), reference of record.

Saunal et al. teaches a transdermal topical formulation employing a solvent, absorption promoting agent, an active, comprising the steroid, nomegestrol, and a film-forming agent. Saunal et al. teaches the composition may contain 0.1 to 20.0% of nomegestrol (See col. 5, line 28). Saunal et al. also teaches the solvent or solubilizing agent may be ethanol or isopropanol(See col. 7, line 13). Sanual et al. also teaches that the weight ratio of the ethanol may be 44% to 84.9% (See particularly col. 7, line 41-46). The film-forming agent is a cellulose derivative, hydroxypropylmethylcellulose, hydroxypropylmethylcellulose succinate acetate, and ethylcellulose. (See col.3, line 58-63). The film-forming agent of Saunal et al. can also be PVP VA, a known polyvinylpyrrolidone derivative (See col. 3, line 67).

Maillo et al. teaches a gel formulation for topical use containing progesterone compounds encompassed nomegesterol, with 20 to 40% of ethyl alcohol, 1 to 4% of polyethylene glycol, and water (See page 9, line 41; also page 18, line 25-40, Example 22).

The references do not expressly teach the amount of nomegestrol as 0.05 to 1% in the composition. The references do not expressly teach film-forming agent as methacrylates, and cellulose. The references do not expressly teach a plasticizing agent such as Labrasol®, a preferred C_8/C_{10} polyoxyethylene glycosyl glyceride herein. The

references do not expressly teach the ratio of water, ethanol, propylene glycol, and Labrasol in preferred the solvent system herein. The references do not expressly teach a method of employing the topical nomegestrol composition to treat progesterone deficiency in a host.

Winters et al. teaches a topical formulation of the steroid, 19-nor progesterone for systemic delivery of active. The formulation has a solvent which may include alcohols (See page 4, line 1-2), film-forming agent such as methacrylates, and cellulose (See page 4, line 8-11), a plasticizing agent such as Labrasol (See page. 4, line 18), and a penetration enhancer.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate the amount of nomegestrol herein and a film-forming agent such as methacrylates and cellulose, and Labrasol into the nomegestrol topical composition of Saunal et al. It would have been obvious to one of ordinary skill in the art at the time the invention was made to adjust the ratio of water, ethanol, propylene glycol, and Labrasol in preferred the solvent system herein.

The employment of nomegestrol as an active agent in a topical pharmaceutical composition with carrier materials herein is motivated because these carrier materials, such as methacrylates and cellulose, and Labrasol, are known pharmaceutical excipients, known to be useful in substantially similar topical pharmaceutical compositions comprising the same and similar active ingredients. The incorporation of known carrier materials into a pharmaceutical composition containing a known active is considered within the skill of the artisan.

The optimization of result effect parameters (e.g., amounts of ingredients) is obvious as being within the skill of the artisan, absent evidence to the contrary. Amounts of composition ingredients employed herein are substantially similar to the prior art.

The instant composition containing nomegestrol would be reasonably expected to be similarly useful to raise progesterone levels in a host, regardless of their status as being menopausal or premenopausal, and treating progesterone deficiency thereby.

Claims 9-10, 13, 16, and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Saunal et al. and Maillo et al. in view of Winters et al. as applied to claims 1, 3, 5-8, 11, 12, 14-15, and 18 above, and further in view of Merck Index (Budavari et al., editor, Merck Index, 12th ed., 1996: page889-890, Compound 5232), Eibl et al. (USPN 5,290,769), and Remington's Pharmaceutical Sciences (Gennaro et al., Remington's Pharmaceutical Sciences, 18th ed., 1990: page 1305), reference of record.

The combination of Saunal et al., Maillo et al., and Winters et al. does not expressly teach the employment of isopropylideneglycerol, copolymer of methacrylic acid and ethyl acrylate, and carbomer in the topical nomegestrol composition. The combination of Saunal et al., Maillo et al., and Winters et al. does not expressly teach the ratio of propylene glycol and isopropylidene glycerol.

The Merck Index teaches that isopropylidene glycerol may be used as a solubilizing or plasticizing agent in pharmaceutical compositions (See page 889-890, Compound 5232).

Eibl et al. teaches the use of copolymer of methacrylic acid and ethyl acrylate as pharmaceutical auxiliary agents in topical formulation (See col 5, line 66 and col. 6, line 19-20).

Remington's Pharmaceutical Sciences teaches that carbomer is useful as a gelling and emulsifying agent in pharmaceutical compositions (See page 1305, col. 1).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate isopropylideneglycerol, copolymer of methacrylic acid and ethyl acrylate, and carbomer into the topical nomegestrol composition.

One of ordinary skill in the art would have been motivated to incorporate isopropylideneglycerol, copolymer of methacrylic acid and ethyl acrylate, and carbomer into the topical nomegestrol composition since isopropylideneglycerol, copolymer of methacrylic acid and ethyl acrylate, and carbomer are known as agents for topical pharmaceutical excipients. Incorporating any known excipients, including isopropylideneglycerol, copolymer of methacrylic acid and ethyl acrylate, and carbomer, into the topical nomegestrol composition would be considered as being within the purview of skilled artisan. Furthermore, the optimization of the amount ratio between propylene glycol and isopropylidene glycerol would be obvious as considered being within the purview of skilled artisan.

Response to Arguments

Applicant's arguments filed August 8, 2006 averring the differences between transdermal preparation and the instant invention have been fully considered but they are not persuasive. Specifically, Applicant argues that "The objective of such a preparation [note: transdermal preparation] is to have a delayed or protracted diffusion of the active ingredient through skin and a transdermal device is not intended to have the product reach the bloodstreams as in Applicant's composition..." [emphasis added]. Examiner notes that the purpose of transdermal preparation is not only to provide a prolonged effect but to deliver the active drug through the skin (i.e., transdermal) so that the active e drugs reach to the systemic circulation, which is contrary to what applicant asserted. Applicant also argues that Applicant's invention is intended to ensure passage of the active ingredient nomegesterol acetate into the bloodstream. It is succinctly clear that the instant invention is a transdermal preparation. Examiner notes that transdermal preparation is not limited to the patch preparation. Transdermal preparation can be lipstick, cream, gel, ointment, as long as these dosage forms can deliver the active drugs effectively through the skin to the systemic bloodstream.

Applicant's arguments filed August 8, 2006 averring examiner using hindsight reasoning have been fully considered but they are not persuasive. In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the

time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). Examiner notes that the secondary references are all directed to the teachings showing the herein claimed excipients as commonly used excipients in formulating topical and/or transdermal composition.

Applicant's remarks filed August 8, 2006 with regard to the difficulties of solubilizing progesterone in general have been considered, but are not found persuasive. Absent evidence to the contrary, using the conventional excipients, which are known to be useful for formulating topical and transdermal preparation, to arrive at the herein claimed preparation is considered obvious as being within the purview of skilled artisans. No such evidence is found herein.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to San-ming Hui whose telephone number is (571) 272-0626. The examiner can normally be reached on Mon 9:00 to 1:00, Tu - Fri from 9:00 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan, PhD., can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

San-ming Hui
Primary Examiner
Art Unit 1617